Please add new claim 5 to read as follows.

A3 5.(New) A cell comprising the expression vector of Claim 1.

RESPONSE

I. Status of the Claims

Claims 1, 2 and 3 have been amended. New Claim 5 has been added. Claims 1-3, and 5 are therefore presently pending in the case. For the convenience of the Examiner, a clean copy of the pending claims is attached hereto as **Exhibit A**. In compliance with 37 C.F.R. § 1.121(c)(1)(ii), a marked up copy of the original claims is attached hereto as **Exhibit B.** A marked up copy of the original title and abstract are attached hereto as **Exhibit C** and clean copy of the amended title and abstract is attached hereto as **Exhibit D.**

II. Support for the Amended Specification and Claims

Claim 1 has been amended to further clarify the claim. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least in Claim 1 and the sequence listing as originally filed.

Claim 2 has been amended to further clarify the claim, and to recite that the stringent hybridization conditions are those used as an example in the specification as filed. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least in Claim 2 as originally filed and on or about page 4, lines 25-29.

Claim 3 has been amended to comply with and Examiner request. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least in Claim 3 and the sequence listing as originally filed.

Claim 5 has been added to better claim the present invention. New Claim 5 is supported by the specification as originally filed with particular support being found on or about page 14 lines 18-24.

As the amendments to claims 1-3 and new Claim 5 are fully supported by the specification and claims as originally filed, they do not constitute new matter. Entry therefore is respectfully requested.

III. Formal Matters

All of the Examiner's requests described in this section have been incorporated into the amended title, abstract and claims.

IV. Objections

The Action objects to the title of the disclosure because it allegedly is not descriptive. Applicants in no way agree. However, in order to progress the application more rapidly towards allowance, Applicants have amended the title of the present application to read: POLYNUCLEOTIDES AND POLYPEPTIDES ENCODING HUMAN ION CHANNEL PROTEINS.

The Action also objects to the abstract of the disclosure because it allegedly fails to disclose any information unique and specific to the elected invention. Applicants in no way agree and submit that abstracts of this type have been acceptable to the U.S.P.T.O. as evidenced at least by the abstracts of issued U.S. Patents Nos: 6,403,784, 6,433,153, 6,441,153, 6,441,154, 6,444,456 and 6,448,388. However, in order to progress the application more rapidly towards allowance Applicants have amended the abstract of the present application to read: Novel human ion channel protein polynucleotide and polypeptide sequences are disclosed that can be used in therapeutic, diagnostic, and pharmacogenomic applications.

In amending both the title and abstract, Applicants have carefully considered the Examiner's remarks. However, as the present application discloses polypeptide sequences and both claims 2 and 3 refers to an amino acid sequence, Applicants have chosen in the interest of accuracy and completeness to include the term "polypeptide" in both the title and abstract.

V. Rejection of Claims Under 35 U.S.C. § 101

The Action first rejects claims 1-3, and 5 under 35 U.S.C. § 101, as allegedly lacking a patentable utility. Applicants respectfully traverse.

The Action states that the specification does not "disclose a specific and substantial biological role" for the claimed sequences (Action at page 3, last paragraph) and yet identifies the present invention as a receptor later in the same paragraph and in several other locations. Applicants disagree, as the presently claimed sequence is clearly referred to as a ion channel protein (see, at least, the title

and specification Section 2), and the sequences are clearly identified on page 3 second paragraph as ion channels and further, that ion channel proteins "mediate or facilitate the passage of materials across the lipid bilayer". Thus the biological role of the presently claimed ion channel protein is well defined, it facilitates the transport of materials, more specifically ions, across the lipid bilayer.

The Action, (page 4, lines 1) also identifies the instant situation as "directly analogous to that addressed in Brenner v. Mason, 148 U.S.P.Q. 689 (Sus. Ct., 1966) in which a novel compound which was structurally analogous to other compounds which were known to possess anticancer activity was alleged to be potentially useful as an antitumor agent". Applicants respectfully disagree with the Action's assertion that this is a direct analogy. An activity, such as anticancer activity, is clearly distinct from a term that defines a molecules function, in the present invention, the term ion channel. Ion channels are well known to have the biological function of transporting ions across membranes through channels. In contrast a term of activity, such as anticancer activity, does not identify a specific function. There are many ways in which a compound can have anticancer activity, it can have one or more of specific functions, such as but not limited to the ability to inhibit enzymes involved in DNA synthesis or repair. It could even, for example increase the activity of a transporter thereby enhancing the ability of a drug to cross the cell membrane. Thus, it is Applicants belief that those of skill in the art would readily recognize that while some might use the terms activity and function interchangeably, that the term activity is also used in a broader sense, such as with the term anticancer activity as used in *Brenner v. Manson.*

The Action also states (page 4, lines 21-23) that "Sequence homology alone cannot be accepted in the absence of supporting evidence, because the relevant literature acknowledges that function cannot be based solely on structural similarity to a protein found in the sequence database." The Action then goes on to present a series of examples.

First the Action cites an article by Skolnick, *et al.* (Trends in Biotech *18*:34-39, 2000) for the proposition that "(k)nowing the protein structure by itself is insufficient to annotate a number of functional classes and is also insufficient for annotating the specific details of protein function" (Skolnick at page 36, emphasis added). However, Skolnick, *et al.* concerns predicting protein function not by overall amino acid homology to other family members, but instead concerns prediction of function based on the presence of certain functional "motifs" present within a given protein sequence. Thus, Skolnick does not apply to the current situation, where overall protein homology is used to assign

function to a particular sequence. However, even in the event that Skolnick is applicable, Skolnick itself concludes that "sequence-based approaches to protein-function prediction have proved to be very useful" (Skolnick at page 37), admitting that such methods have correctly assigned function in 50-70% of the cases, thus a majority of the time supporting rather than refuting Applicants assertions.

The Action next cites Bork (Genome Research *10*:398-400, 2000) as supporting the proposition that prediction of protein function from homology information is somewhat unpredictable. The Action directs attention to page 399, on which the author notes the limitations of various methods of analysis. It is of interest that in his "analysis" Bork often uses citations to many of his own previous publications, an interesting approach. ' My position is supported by my previous disclosures of my position.' If Bork's position is supported by others of skill in the art, one would expect that he would reference them rather than himself to provide support for his statements. Given that the standard with regard to obtaining U.S. patents is those of skill in the art, this observation casts doubt on the broad applicability of Bork's position. It should also be noted that in Table 1, on page 399, in which selected examples of prediction accuracy are presented, that the reported accuracy of the methods which Applicants have employed are, in fact, very high. While nowhere in Bork is there a comparison of the prediction accuracy based on the percentage homology between two proteins or two classes of proteins, " Homology (several methods)" is assigned an accuracy rate of 98% and "Functional features by homology" is assigned an accuracy rate of 90%. Given that these figures were obtained based on what is at least a 4 year old analysis, these high levels of accuracy would appear to support rather than refute Applicants assertions in the present case. Additionally Bork even states (on page 400, second column, line 17) that " However, there is still no doubt that sequence analysis is extremely powerful". In summary, it is clear that it is not Bork's intention to refute the value of sequence analysis but rather he is indicating that there is room for improvement .

The action next cites Doerks *et al.* (Trends in Genetics *14*:248-250, 1998) in support that sequence-to-function methods of assigning protein function are prone to errors due to partial annotation, multifunctionality and over prediction. However, Doerks *et al.* states that "utilization of family information and thus a more detailed characterization" should lead to "simplification of update procedures for the entire families if functional information becomes available for at least one member" (Doerks *et al.*, page 248, paragraph bridging columns 1 and 2, emphasis added). Applicants point out that transporters represent a well-studied protein family with a large amount of known functional

information, exactly the situation that Doerks *et al.* suggests will "simplify" and "avoid the pitfalls" of previous sequence-to-function methods of assigning protein function (Doerks *et al.*, page 248, columns 1 and 2). Thus, instead of supporting the Action's position against utility, Doerks *et al.* supports Applicants' position that the presently claimed sequences have a recognized substantial and credible utility.

The Examiner also cites Smith, *et al.* (Nature Biotechnology *15*:1222-1223, 1997) as teaching "that there are numerous cases in which proteins of very different functions are homologous" (Action at page 5). However, the Smith, *et al.* article also states "the major problems associated with nearly all of the current automated annotation approaches are - paradoxically - minor database annotation inconsistencies (and a few outright errors)" (page 1222, second column, first paragraph, emphasis added). Thus, Smith, *et al.* do not in fact seem to stand for the proposition that prediction of function based on homology is fraught with uncertainty, and thus also does not support the alleged lack of utility.

The Examiner next cites Brenner (Trends in Genetics *15*:132-133, 1999) as teaching that proposition that accurate inference of function from homology is a difficult problem. However, this statement is based on the assumption that "if there are only 1000 superfamilies in nature, then most homologs must have different molecular and cellular functions" (page 132, second column). Furthermore, Brenner suggests that one of the main problems in using homology to predict function is "an issue solvable by appropriate use of modern and accurate sequence comparison procedures" (page 132, second column), and in fact references an article by Altschul *et al.*, which is the basis for one of the "modern and accurate sequence comparison procedures" used by Applicants. Thus, the Brenner article also does not support the alleged lack of utility.

Finally, the Action finally cites Bork *et al.* (Trends in Genetics *12*:425-427, 1996) as supporting the proposition that prediction of protein function from homology information is somewhat unpredictable. The question as to whether Bork's positions are generally supported by those of skill in the art was discussed above in the paragraph regarding the other Bork citation. It should also be noted that this article was published approximately 6 years ago and thus refers to errors or "traps" associated with earlier algorithms and technologies in a field that has undergone constant improvement. This publication identifies (Table 1) various areas in which incorrect information appears in sequence databases. These "traps" include Synonyms - a single gene having a variety of names, Different gene-same name- when the same name is used to describe different genes, Spelling errors, Contamination-

the unintentional inclusion of vector sequences, etc. and propagation of incorrect functional associations based on poorly analyzed homology. All of these issues can effect the accuracy of sequence base analysis, however all can be overcome by a more careful analysis as would be done by one of skill in the art. Automatic methods of sequence homology as identified by any algorithm is a staring point for consideration, and one of skill in the art can then through further analysis, structure - function analysis, etc. can and should then verify the associations. For example in addition to algorithm based sequence analysis the sequences of the present invention underwent careful analysis by a series of individuals of skill in the art, many highly qualified (2 experienced B.S. and 3 Ph.D. level scientists). Clearly such highly skilled and careful analysis reduces the influence of such "traps". Furthermore, in the final section of this publication (page 427) it again becomes cleat that Bork et al. do not discount the value of sequence analysis "we wish to point out that sequence database are the most useful tool in sequence analysis and the question should be how can one further improve their value". Thus clearly this publication represents a call to action to enhance the already high value of sequence analysis rather than an indictment of the utility of sequence based analysis. Therefore, as Bork *et al.* identifies the high value of sequence based analysis it actually supports rather than refutes Applicants assertions regarding the utility of the present invention.

In summary a careful reading of the cited "relevant literature" does not in fact support the concept that function cannot be based on sequence and structural similarity, in contrast many of the examples actually support the use of such methodologies while identifying several areas in which caution should be exercised. As stated previously these inaccuracies and potential pitfalls can be overcome by a more careful analysis by those of skill in the art. Automatic methods of sequence homology identification was only the staring point for consideration the sequences of the present invention underwent careful analysis by a series of individuals of skill in the art, many highly qualified (2 experienced B.S. and 3 Ph.D. level scientists).

Applicants respectfully submit that the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. As set forth by the Federal Circuit, "(t)he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that "(t)o violate § 101 the claimed device

must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (224 USPQ 739 (Fed. Cir. 1985); "*Cross*") states "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101". *Cross* at 748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable *(State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in *Diamond vs. Chakrabarty*, 206 USPQ 193 (S.Ct. 1980)).

In *In re Brana,* (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*"), the Federal Circuit admonished the P.T.O. for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an

incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted. The Examiner states that a "real-world" utility "does not require further research" (Action at page 4). However, even if, *arguendo*, further research might be required in certain aspects of the present invention, this does not preclude a finding that the invention has utility, as set forth by the Federal Circuit's holding in *Brana*, which clearly states, as highlighted in the quote above, that "pharmaceutical inventions, necessarily includes the expectation of <u>further research and development</u>" (*Brana* at 1442-1443, emphasis added). In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands, supra.*

The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. According to the Examination Guidelines for the Utility Requirement, if the applicant has asserted that the claimed invention is useful for any particular purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, the Examiner should not impose a rejection based on lack of utility (66 Federal Register 1098, January 5, 2001).

As evidence of the credibility of Applicants assertion that the present invention is a ion channel, in particular a shorter variant of KCNA7. Applicants submit a nucleic acid sequence comparison between SEQ ID NO:1 and GenBank accession no. AF315818 (**Exhibit E**) which has been annotated by third party scientists, wholly unaffiliated with Applicants, as encoding *Homo sapiens* voltage-gated potassium channel KCNA7 mRNA (**Exhibit F**). After the first 38 bases, this molecule SEQ ID NO:1 is 99.927 % identical to that internal portion of AF315818 which encodes the variant of the present invention.

Given this clear and convincing evidence that those of skill in the art would recognize the present invention as an ion channel protein, more specifically a variant of KCNA7, whose function is described in the scientific publications entitled "Characterization of the human voltage-gated potassium channel gene, KCNA7, a candidate gene for inherited cardiac disorders, and its exclusion as cause of progressive familial heart block I (PFHBI)."(Bardien-Kruger, S., *et al.*, Eur J Hum Genet, 10(1):36-43, 2002). Thus clearly, there can be no question that Applicants' asserted utility for the described sequences is "credible." Applicants have thus supplied evidence supporting their assertion that those of skill in the art would recognize that the sequences of the present invention encode a ion channel protein, more particularly that of KCNA7 and has all the recognized uses thereof. In contrast, the Examiner has provided no evidence of record indicating that those of skill in the art would not recognize the sequences of the present invention encode an ion channel protein. As such, the scientific evidence clearly establishes that Applicants have described an invention whose utility is in full compliance with the provisions of 35 U.S.C. § 101, and the Examiner's rejection should be withdrawn.

As still another example of utility of the present nucleotide sequences, Applicants point out that, as taught in the specification as originally filed the claimed polynucleotide sequences can be used to track the expression of the genes encoding the described proteins. In particular, the specification describes how the described sequences can be represented using a gene chip format to provide a high throughput analysis of the level of gene expression. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776. Evidence of the "real world" substantial utility of the present invention is provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Agilent Technologies, Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company, Rosetta Inpharmatics, was viewed to have such "real world" value (net equity value of the transaction was $620 million) that it was acquired by large pharmaceutical company, Merck & Co., for significant sums of money. The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. The sequences of the present invention describe a novel gene encoding a GPCR and provide a unique identifier of the

corresponding gene. Such gene chips clearly have utility, as evidenced by hundreds of issued U.S. Patents, such as U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776. The present nucleotide sequences clearly encode human GPCRs, as detailed throughout the specification. The specification also teaches that GPCRs are associated with a wide variety of cellular functions, and as such, that GPCR interacting proteins have been subject to intense scrutiny as potential drug targets. Therefore, as the present sequences are specific markers of the human genome, and such specific markers are targets for the discovery of drugs that are associated with human disease, those of skill in the art would instantly recognize that the present nucleotide sequences would be an ideal, novel candidate for assessing gene expression using such gene chips. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequences, must in themselves be useful. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

An additional utility of the present invention is in expanding the utility of data coming from the human genome project. Persons of skill in the art, as well as thousands of venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. All current therapeutics used in humans directly or indirectly interact with biological sequences encoded by the human genome, and virtually all future human therapeutics shall do likewise. Consequently, billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, Science *291*:1304). The results have been a stunning success, as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, Science *291*:1153). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years).

Although Applicants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), as a further example of the utility of the presently claimed polynucleotide, the present nucleotide sequence has a specific utility in mapping the protein encoding regions of the corresponding human chromosome, as detailed in the specification Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of the human

chromosome containing the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, s Only a minor percentage of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). The Applicants respectfully submit that the practical scientific value of expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. For further evidence in support of the Applicants' position, the Board is requested to review, for example, section 3 of Venter *et al.* (*supra at* pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article.

As evidence of the specific utility of the sequences of the present invention in localizing the specific region of the human chromosome and identification of functionally active intron/exon splice junctions is the information provided in **Exhibit G**. This is the result of a blast analysis using SEQ ID NO:1 of the present invention when compared to the identified human genomic sequence. This result indicates that the sequence of the present invention is encoded by 2 exons spread non-contiguously along a region of human chromosome (19q13.3), which is represented by clone AC008687.5. Thus clearly one would not simply be able to identify the protein encoding exons that make up the sequence of the present intention, nor to map the protein encoding regions identified specifically by the sequences of the present invention without knowing exactly what those specific sequences were. Additionally, it should be noted that the gene of AF315818 (**Exhibit F**), *Homo sapiens* voltage-gated potassium

channel KCNA7 mRNA also maps to the same region of human chromosome 19 (essentially position 49.2M on 19q13.3). This further supports Applicant's position that the sequences of the present invention encode a variant of the human *Homo sapiens* voltage-gated potassium channel KCNA7.

Finally, the requirements set forth in the Action for compliance with 35 U.S.C. § 101 do not comply with the requirements set forth by the Patent and Trademark Office ("the PTO") itself for compliance with 35 U.S.C. § 101. The PTO has issued numerous patents on polynucleotide sequences that have not been directly shown to be associated with the function of the protein that is set forth in the specification, or a direct association between the claimed sequences and a particular "biological significance" (Action at page 4), the conditions apparently set forth by the Examiner as allegedly necessary to comply with 35 U.S.C. § 101. The Examiner is invited to review U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,2812 (each of which claims short polynucleotide fragments), and recently issued U.S. Patent No. 6,340,583 (which includes no working examples). None of these issued U.S. Patents contain examples of the "real-world" utilities that the Examiner seems to be requiring in the present Action. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section IV below), Applicants submit that the presently claimed polynucleotide must also meet the requirements of 35 U.S.C. § 101 and that any other decision is both arbitrary and capricious.

For each of the foregoing reasons, Applicants submit that as the presently claimed nucleic acid molecules have been shown to have a substantial, specific, credible and well-established utility, the rejection of claims 1-3, and 5 under 35 U.S.C. § 101 has been avoided, and respectfully request that the rejection be withdrawn.

VI. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

The Action rejects claims 1-3, and 5 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

Applicants submit that claims 1-3, and 5 have been shown to have "a specific, substantial, and credible utility", as detailed in the section above. Applicants therefore request that the rejection of claims 1-3, and 5 under 35 U.S.C. § 112, first paragraph, be withdrawn.

VII. Rejection of Claim 2 Under 35 U.S.C. § 112, Second Paragraph

The Action next rejects Claim 2 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Action rejects Claim 2 as allegedly indefinite based on the term "stringent" in regards to hybridization conditions. While Applicants submit that the term is sufficiently definite, as a number of stringent hybridization conditions are defined in the specification and would be known to those of skill in the art, solely in order to progress the case more rapidly toward allowance the claim has been revised to recite the exact hybridiation conditions described as an example in the specification as originally filed. Applicants submit that revised Claim 2 even more clearly meets the requirements of 35 U.S.C. § 112, second paragraph. Applicants stress that "a claim need not 'describe' the invention, such description being the role of the disclosure". *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). Based on the foregoing, Applicants submit that Claim 2 is sufficiently definite, and respectfully request withdrawal of this rejection.

VIII. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Landsman have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

04/17/03
Date

Lance K. Ishimoto by David W. Hibler DAVID W. HIBLER Reg. No. 41,071

Lance K. Ishimoto Reg. No. 41,866

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Exhibit A
Clean Version of The Pending Claims in
U.S. Patent Application Ser. No. 09/974,712

1. (Amended) An expression vector comprising the nucleotide sequence of SEQ ID NO: 1

2. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence of SEQ ID NO:2; and

(b) hybridizes under stringent conditions including washing in 0.1xSSC/0.1% SDS at 68°C to the full complement of the nucleotide sequence of SEQ ID NO: 1.

3. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 2.

5.(New) A cell comprising the expression vector of Claim 1.

Exhibit B
Marked Up Version of Amended Claims in
U.S. Patent Application Ser. N . 09/974,712

1. (Amended) An [isolated polynucleotide] expression vector comprising the nucleotide sequence [described in] of SEQ ID NO: 1

2. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence [shown in] of SEQ ID NO:2; and

(b) hybridizes under stringent conditions including washing in 0.1xSSC/0.1% SDS at 68°C to the full complement of the nucleotide sequence of SEQ ID NO: 1.

3. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence [shown in] of SEQ ID NO: 2.

4. (Cancelled) An isolated oligopeptide having a sequence of at least about 12 contiguous amino acids first disclosed in SEQ ID NO:2.

5.(New) A cell comprising the expression vector of Claim 1.

Exhibit C
Marked Up Version of Amended Title and Abstract in U.S. Patent Application Ser. No. 09/974,712

Title

POLYNUCLEOTIDES AND POLYPEPTIDES ENCODING [NOVEL] HUMAN ION CHANNEL PROTEINS [AND POLYNUCLEOTIDES ENCODING THE SAME]

Abstract

Novel human ion channel protein polynucleotide and polypeptide sequences are disclosed that can be used in therapeutic, diagnostic, and pharmacogenomic applications.

Exhibit D
Clean Version of Amended Title and Abstract in U.S. Patent Application Ser. No. 09/974,712

Title

POLYNUCLEOTIDES AND POLYPEPTIDES ENCODING HUMAN ION CHANNEL PROTEINS

Abstract

Novel human ion channel protein polynucleotide and polypeptide sequences are disclosed that can be used in therapeutic, diagnostic, and pharmacogenomic applications.

EXHIBIT E

Nucleic acid sequence comparison between SEQ ID NO:1 and Accession No.AF315818

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FASTA searches a protein or DNA sequence data bank
 version 3.3t05 March 30, 2000
Please cite:
 W.R. Pearson & D.J. Lipman PNAS (1988) 85:2444-2448

/tmp/fastaCAAIqaGqw: 1371 nt

 >seqid1
 vs  /tmp/fastaDAAJqaGqw library
searching /tmp/fastaDAAJqaGqw library

   1447 residues in     1 sequences

FASTA (3.34 January 2000) function [optimized, +5/-4 matrix (5:-4)] ktup: 6
 join: 62, opt: 47, gap-pen: -16/ -4, width:  16
 Scan time:  0.083
The best scores are:                                                opt
AF315818 ACCESSION:AF315818 NID: gi 14485554 g (1447) [f] 6846
AF315818 ACCESSION:AF315818 NID: gi 14485554 g (1447) [r]  100

>>AF315818 ACCESSION:AF315818 NID: gi 14485554 gb AF3158  (1447 nt)
 initn: 6846 init1: 6846 opt: 6846
 99.927% identity in 1371 nt overlap (1-1371:38-1408)


                                              10        20        30
seqid1                                  ATGGAGCCGCGGTGCCCGCCGCCGTGCGGC
                                        ::::::::::::::::::::::::::::::
AF3158 GGTTCGCGGGTCGCCGGGGCTGCGCGCGCCATGGAGCCGCGGTGCCCGCCGCCGTGCGGC
        10         20         30         40         50         60

               40         50         60         70         80         90
seqid1 TGCTGCGAGCGGCTGGTGCTCAACGTGGCCGGGCTGCGCTTCGAGACGCGGGCGCGCACG
       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
AF3158 TGCTGCGAGCGGCTGGTGCTCAACGTGGCCGGGCTGCGCTTCGAGACGCGGGCGCGCACG
        70         80         90        100        110        120

              100        110        120        130        140        150
seqid1 CTGGGCCGCTTCCCGGACACTCTGCTAGGGGACCCAGCGCGCCGCGGCCGCTTCTACGAC
       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
AF3158 CTGGGCCGCTTCCCGGACACTCTGCTAGGGGACCCAGCGCGCCGCGGCCGCTTCTACGAC
       130        140        150        160        170        180

              160        170        180        190        200        210
seqid1 GACGCGCGCCGCGAGTATTTCTTCGACCGGCACCGGCCCAGCTTCGACGCCGTGCTCTAC
       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
AF3158 GACGCGCGCCGCGAGTATTTCTTCGACCGGCACCGGCCCAGCTTCGACGCCGTGCTCTAC
       190        200        210        220        230        240

              220        230        240        250        260        270
seqid1 TACTACCAGTCCGGTGGGCGGCTGCGGCGGCCGGCGCACGTGCCGCTCGACGTCTTCCTG
       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
AF3158 TACTACCAGTCCGGTGGGCGGCTGCGGCGGCCGGCGCACGTGCCGCTCGACGTCTTCCTG
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                280       290       300       310       320       330
seqid1 GAAGAGGTGGCCTTCTACGGGCTGGGCGCGGCGGCCCTGGCACGCCTGCGCGAGGACGAG
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       310       320       330       340       350       360

                340       350       360       370       380       390
seqid1 GGCTGCCCGGTGCCGCCCGAGCGCCCCCTGCCCCGCCGCGCCTTCGCCCGCCAGCTGTGG
       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
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       370       380       390       400       410       420

                400       410       420       430       440       450
seqid1 CTGCTTTTCGAGTTTCCCGAGAGCTCTCAGGCCGCGCGCGTGCTCGCCGTAGTCTCCGTG
       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
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       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
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                700       710       720       730       740       750
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       730       740       750       760       770       780

                760       770       780       790       800       810
seqid1 CTTCCCTACTTTGTGGCACTGGGCACCGAGCTGGCCCGGCAGCGAGGGGTGGGCCAGCAG
       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
AF3158 CTTCCCTACTTTGTGGCACTGGGCACCGAGCTGGCCCGGCAGCGAGGGGTGGGCCAGCAG
       790       800       810       820       830       840

                820       830       840       850       860       870
seqid1 GCCATGTCACTGGCCATCCTGAGAGTCATCCGATTGGTGCGTGTCTTCCGCATCTTCAAG
       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
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               880       890       900       910       920       930
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       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
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       910       920       930       940       950       960

               940       950       960       970       980       990
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       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
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              1000      1010      1020      1030      1040      1050
seqid1 TACTTTGCCGAAGTTGACCGGGTGGACTCCCATTTCACTAGCATCCCTGAGTCCTTCTGG
       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
AF3158 TACTTTGCCGAAGTTGACCGGGTGGACTCCCATTTCACTAGCATCCCTGAGTCCTTCTGG
      1030      1040      1050      1060      1070      1080

              1060      1070      1080      1090      1100      1110
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       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
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              1120      1130      1140      1150      1160      1170
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       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
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              1180      1190      1200      1210      1220      1230
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              1240      1250      1260      1270      1280      1290
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       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
AF3158 GGGATGTTCAGCCATGTGGACATGCAGCCTTGTGGCCCACTGGAGGGCAAGGCCAATGGG
      1270      1280      1290      1300      1310      1320

              1300      1310      1320      1330      1340      1350
seqid1 GGGCTGGTGGACGGGGAGGTACCTGAGCTACCACCTCCACTCTGGGCACCCCCAGGGAAA
       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
AF3158 GGGCTGGTGGACGGGGAGGTACCTGAGCTACCACCTCCACTCTGGGCACCCCCAGGGAAA
      1330      1340      1350      1360      1370      1380

              1360      1370
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       :::::::::::::::::::::
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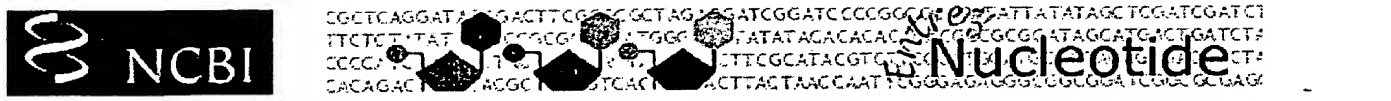

☐ 1: AF315818. Homo sapiens volt...[gi:14485554] Links

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DEFINITION  Homo sapiens voltage-gated potassium channel KCNA7 mRNA, complete
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ACCESSION   AF315818
VERSION     AF315818.1  GI:14485554
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 1447)
  AUTHORS   Bardien-Kruger,S., Wulff,H., Arieff,Z., Brink,P., Chandy,K.G. and
            Corfield,V.
  TITLE     Characterization of the human voltage-gated potassium channel gene,
            KCNA7, a candidate gene for inherited cardiac disorders, and its
            exclusion as cause of progressive familial heart block I (PFHBI)
  JOURNAL   Unpublished
REFERENCE   2  (bases 1 to 1447)
  AUTHORS   Bardien-Kruger,S., Wulff,H., Arieff,Z., Brink,P., Chandy,K.G. and
            Corfield,V.
  TITLE     Direct Submission
  JOURNAL   Submitted (23-OCT-2000) SANBI, University of Western Cape,
            Modderdam Road, Cape Town 7535, South Africa
FEATURES             Location/Qualifiers
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                     /chromosome="19"
                     /map="19q13.3"
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                     /db_xref="GI:14485555"
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                     RGRFYDDARREYFFDRHRPSFDAVLYYYQSGGRLRRPAHVPLDVFLEEVAFYGLGAAA
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                     CLETLPDFRDDRDGTGLAAAAAAGPFPAPLNGSSQMPGNPPRLPFNDPFFVVETLCIC
                     WFSFELLVRLLVCPSKAIFFKNVMNLIDFVAILPYFVALGTELARQRGVGQQAMSLAI
                     LRVIRLVRVFRIFKLSRHSKGLQILGQTLRASMRELGLLIFFLFIGVVLFSSAVYFAE
                     VDRVDSHFTSIPESFWWAVVTMTTVGYGDMAPVTVGGKIVGSLCAIAGVLTISLPVPV
                     IVSNFSYFYHRETEGEEAGMFSHVDMQPCGPLEGKANGGLVDGEVPELPPPLWAPPGK
                     HLVTEV"
BASE COUNT      204 a    480 c    451 g    312 t
ORIGIN
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    121 gcgcacgctg ggccgcttcc cggacactct gctaggggac ccagcgcgcc gcggccgctt
    181 ctacgacgac gcgcgccgcg agtatttctt cgaccggcac cggcccagct tcgacgccgt
    241 gctctactac taccagtccg gtgggcggct gcggcggccg gcgcacgtgc cgctcgacgt
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   1321 caatgggggg ctggtggacg gggaggtacc tgagctacca cctccactct gggcaccccc
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   1441 ccctaga
//
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Exhibit G
Nucleic acid comparison of SEQ ID NO:1 vs. Human Genome

MEGABLAST 1.2.3-Paracel [2001-11-20]
Reference:
Zheng Zhang, Scott Schwartz, Lukas Wagner, and Webb Miller (2000),
"A greedy algorithm for aligning DNA sequences",
J Comput Biol 2000; 7(1-2):203-14.
Database: Homo_sapiens.latestgp.masked.fa
44,521 sequences; 200,768,834,160 total letters

Query= 251seqid1
(1371 letters)

Sequences producing significant alignments:	Score (bits)	E Value
AC008687.5.1.157633	1612	0.0
AC005906.1.1.185952	157	2e-35
AC005833.1.1.122903	157	2e-35
AL365361.11.1.155343	129	5e-27
AC006063.1.1.150001	94	3e-16
AL358215.16.1.101529	84	3e-13

>AC008687.5.1.157633
Length = 157633

Score = 1612 bits (813), Expect = 0.0
Identities = 816/817 (99%)
Strand = Plus / Minus

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              |||||||||||| ||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 82187 gttccccgctccgctgaatggctccagccaaatgcctggaaatccaccccgcctgccctt 82128


Query: 615   caatgacccgttcttcgtggtggagacgctgtgtatttgttggttctcctttgagctgct 674
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 82127 caatgacccgttcttcgtggtggagacgctgtgtatttgttggttctcctttgagctgct 82068


Query: 675   ggtacgcctcctggtctgtccaagcaaggctatcttcttcaagaacgtgatgaacctcat 734
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 82067 ggtacgcctcctggtctgtccaagcaaggctatcttcttcaagaacgtgatgaacctcat 82008


Query: 735   cgattttgtggctatccttccctactttgtggcactgggcaccgagctggcccggcagcg 794
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Query: 795   aggggtgggccagcaggccatgtcactggccatcctgagagtcatccgattggtgcgtgt 854
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Sbjct: 81947 aggggtgggccagcaggccatgtcactggccatcctgagagtcatccgattggtgcgtgt 81888


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Query: 975    cttttccagcgccgtctactttgccgaagttgaccgggtggactcccatttcactagcat 1034
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Query: 1035   ccctgagtccttctggtgggcggtagtcaccatgactacagttggctatggagacatggc 1094
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Query: 1095   acccgtcactgtgggtggcaagatagtgggctctctgtgtgccattgcgggcgtgctgac 1154
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Query: 1215   agagggcgaagaggctgggatgttcagccatgtggacatgcagccttgtggcccactgga 1274
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Query: 1335   ggcacccccagggaaacacctggtcaccgaagtgtga 1371
              |||||||||||||||||||||||||||||||||||
Sbjct: 81407  ggcacccccagggaaacacctggtcaccgaagtgtga 81371


 Score = 1100 bits (555), Expect = 0.0
 Identities = 555/555 (100%)
 Strand = Plus / Minus


Query: 1      atggagccgcggtgcccgccgccgtgcggctgctgcgagcggctggtgctcaacgtggcc 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Query: 61     gggctgcgcttcgagacgcgggcgcgcacgctgggccgcttcccggacactctgctaggg 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Query: 121    gacccagcgcgccgcggccgcttctacgacgacgcgcgccgcgagtatttcttcgaccgg 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 83773  gacccagcgcgccgcggccgcttctacgacgacgcgcgccgcgagtatttcttcgaccgg 83714
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Query: 181   caccggcccagcttcgacgccgtgctctactactaccagtccggtgggcggctgcggcgg 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 83713 caccggcccagcttcgacgccgtgctctactactaccagtccggtgggcggctgcggcgg 83654

Query: 241   ccggcgcacgtgccgctcgacgtcttcctggaagaggtggccttctacgggctgggcgcg 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Query: 301   gcggccctggcacgcctgcgcgaggacgagggctgcccggtgccgcccgagcgccccctg 360
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Query: 361   ccccgccgcgccttcgcccgccagctgtggctgcttttcgagtttcccgagagctctcag 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Query: 421   gccgcgcgcgtgctcgccgtagtctccgtgctggtcatcctcgtctccatcgtcgtcttc 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 83473 gccgcgcgcgtgctcgccgtagtctccgtgctggtcatcctcgtctccatcgtcgtcttc 83414

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Sbjct: 83413 tgcctcgagacgctgcctgacttccgcgacgaccgcgacggcacggggcttgctgctgca 83354

Query: 541   gccgcagccggcccg 555
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>AC005906.1.1.185952
          Length = 185952

 Score =  157 bits (79), Expect = 2e-35
 Identities = 168/197 (85%), Gaps = 3/197 (1%)
 Strand = Plus / Minus


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Sbjct: 108035 tggg-cagcaggccatgtccctggccatcctccgagtcatccgcctggtccgggtgttcc
107977


Query: 860     gcatcttcaagctgtcccggcactcaaagggcctgcaaatcttgggccagacgctt-cgg 918
                |||||||||||| ||||| ||||| ||||| ||| ||||| |||| ||| | |
Sbjct: 107976 gcatcttcaagctctcccgccactccaaggggctgcagatcctgggcaagac-cttgcag
107918


Query: 919     gcctccatgcgtgagctgggcctcctcatctttttcctcttcatcggtgtggtcctcttt 978
                ||||||||| | |||||||| || |||||||| |||||||||||||| ||  |||||||
```

```
Sbjct: 107917 gcctccatgagggagctggggctgctcatcttcttcctcttcatcggggtcatcctcttc
107858


Query: 979    tccagcgccgtctactt 995
               ||||| ||||||||||
Sbjct: 107857 tccagtgccgtctactt 107841


 Score =  137 bits (69), Expect = 2e-29
 Identities = 166/197 (84%), Gaps = 8/197 (4%)
 Strand = Plus / Minus


Query: 1019   cccatttcactagcatccctga-gtccttctggtgggcggtagtcaccatgactacagtt 1077
               |||||||| |||||||||||| | |||||||||||| || |||||||||| || ||
Sbjct: 107817 cccatttctctagcatccctgacg-ccttctggtgggcagtggtcaccatgaccactgtg
107759


Query: 1078   ggctatggagacatg-gcacccgtcactgt-gggtggcaagatagtgggctctctgtgtg 1135
               ||||| || |||||| |  ||| ||||||| ||| |||||||| |||||||| |||||||
Sbjct: 107758 ggctacggggacatgagg-cccatcactgttggg-ggcaagatcgtgggctcgctgtgtg
107701


Query: 1136   ccattgc-gggcgtgctgactatttccctgccagtgcccgtcattgtctccaatttcagc 1194
               |||| || ||| || || || ||| ||||||| |||||||||| |||||||| |||| |
Sbjct: 107700 ccatcgccggg-gtcctcaccattgccctgcctgtgcccgtcatcgtctccaacttcaac
107642


Query: 1195   tacttttatcaccggga 1211
               ||||| || ||||||||
Sbjct: 107641 tacttctaccaccggga 107625


 Score = 77.8 bits (39), Expect = 2e-11
 Identities = 74/85 (87%), Gaps = 4/85 (4%)
 Strand = Plus / Minus


Query: 162    cgagtatttcttcgaccggc-accggcccagcttcgacgccgtgctctactactaccagt 220
               |||||| |||||||||| || |||||||||||||||||   | ||||||||||||||||
Sbjct: 108719 cgagtacttcttcgacc-gcaaccggcccagcttcgacggtatcctctactactaccagt
108661


Query: 221    ccggtgggcggc-tgcggcggccgg 244
               |||| |||| || ||||| ||||||
Sbjct: 108660 ccgg-gggccgcctgcggaggccgg 108637


>AC005833.1.1.122903
          Length = 122903

 Score =  157 bits (79), Expect = 2e-35
 Identities = 168/197 (85%), Gaps = 3/197 (1%)
```

Strand = Plus / Plus

```
Query: 800    tgggccagcaggccatgtcactggccatcctgagagtcatccgattggtgcgtgtcttcc 859
              |||| |||||||||||||| |||||||||| |||||||||  |||| || || ||||
Sbjct: 116136 tggg-cagcaggccatgtccctggccatcctccgagtcatccgcctggtccgggtgttcc
116194


Query: 860    gcatcttcaagctgtcccggcactcaaagggcctgcaaatcttgggccagacgctt-cgg 918
              |||||||||||| ||||| ||||| ||||| ||||| ||| ||||| |||| ||| | |
Sbjct: 116195 gcatcttcaagctctcccgccactccaaggggctgcagatcctgggcaagac-cttgcag
116253


Query: 919    gcctccatgcgtgagctgggcctcctcatcttttttcctcttcatcggtgtggtcctcttt 978
              ||||||||| | |||||||| || |||||||| |||||||||||||| ||  |||||||
Sbjct: 116254 gcctccatgagggagctggggctgctcatcttcttcctcttcatcggggtcatcctcttc
116313


Query: 979    tccagcgccgtctactt 995
              ||||| ||||||||||
Sbjct: 116314 tccagtgccgtctactt 116330
```

Score = 87.7 bits (44), Expect = 2e-14
Identities = 149/182 (81%), Gaps = 12/182 (6%)
Strand = Plus / Plus

```
Query: 162    cgagtatttcttcgaccggc-accggcccagcttcgacgccgtgctctactactaccagt 220
              |||||| |||||||||| || |||||||||||||||||| | ||||||||||||||||
Sbjct: 115389 cgagtacttcttcgacc-gcaaccggcccagcttcgacgccatcctctactactaccagt
115447


Query: 221    ccggtgggcggc-tgcggcggccggcgca-cgtgccgctcgacgtcttcctggaagaggt 278
              | || |||| || ||||| ||||||  || |||||| || ||| | |||||||| ||| |
Sbjct: 115448 ctgg-gggccgcctgcggaggccggt-caacgtgcccctggacattttcctggaggagat
115505


Query: 279    g-gccttctacgggctgggcg-cggcggccctggcacgcctgc-gcgaggacgagggctg 335
                || ||||||  |||||| | ||  |||||||||  |||| | | ||||||||||||||
Sbjct: 115506 ccgc-ttctaccagctgggggacga-ggccctggcg-gccttccgggaggacgagggctg
115562


Query: 336    cc 337
              ||
Sbjct: 115563 cc 115564
```

```
>AL365361.11.1.155343
          Length = 155343
```

Score = 129 bits (65), Expect = 5e-27
Identities = 166/199 (83%), Gaps = 4/199 (2%)

```
 Strand = Plus / Minus


Query: 805    cagcaggccatgtcactggccatcctgagagtcatccgattggtgcgtgtcttccgcatc 864
               ||||||||||||||| ||||||||||||||| ||||||||  ||||  | ||||||||||||
Sbjct: 120617 cagcaggccatgtctctggccatcctgagggtcatccgcctggtaagggtcttccgcatc
120558


Query: 865    ttcaagctgtcccggcactcaaagggcctgcaaat-cttgggccagacgcttcgggcctc 923
               |||||||||||  || |||||  |||||  |||||  || || |||  || |||||   ||| ||
Sbjct: 120557 ttcaagctgtcgcgccactccaaggggctgcagatcctcggg-caaacgctgaaggcgtc
120499


Query: 924    catgcgtgagctgggcctcctcatcttttttcctcttcatcggtgtggtcctcttt-tcca 982
               ||||||  ||||||||  | ||||||||  ||||||||  || || ||  ||||  |||  ||||
Sbjct: 120498 catgcgggagctgggattgctcatcttcttcctctttattggggtcatcct-tttctcca
120440


Query: 983    gcgccgtctactttgccga 1001
               ||||  ||||||||||||||
Sbjct: 120439 gcgcggtctactttgccga 120421


 Score =  119 bits (60), Expect = 5e-24
 Identities = 141/167 (84%), Gaps = 6/167 (3%)
 Strand = Plus / Minus


Query: 349    gagcgccccctgccccgccgcgccttcgcc-cgccagctgtggctgcttttcgagtttcc 407
               |||||  |||  |||||||||||||  ||||  |  ||||||  ||||||||||  |||||||  ||
Sbjct: 121058 gagcggcccttgccccgccgcgacttc-cagcgccaggtgtggctgctcttcgagtaccc
121000


Query: 408    cgagagctctcaggccgcgcgcgtg-c-tcgccgtagtctccgtgctggtcatcctcgtc 465
               |||||||||  |  |||||  ||  ||  |  |  |||||  |  ||  ||||||||||||||||||  ||
Sbjct: 120999 cgagagctc-cgggccg-gcccggggcatcgccatcgtgtccgtgctggtcatcctcatc
120942


Query: 466    tccatcgtcgtcttctgcctcgagacgctgcctgacttccgcgacga 512
               |||||  |||  ||||||||||  ||||||||||  ||  ||||||||||
Sbjct: 120941 tccattgtcatcttctgcctggagacgctgccggagttccgcgacga 120895


 Score = 85.7 bits (43), Expect = 7e-14
 Identities = 158/195 (81%), Gaps = 8/195 (4%)
 Strand = Plus / Minus


Query: 1030  agcatccctga-gtccttctggtgggcggtagtcaccatgactacagttggctatggaga 1088
              ||||||||  ||  |  ||||||||||||||  ||  |||  |||||||  ||  ||  ||||||||||
Sbjct: 50575 agcatcccagatg-ccttctggtgggcagtcgtctccatgacaactgtaggctatggaga 50517


Query: 1089  catggcacccgtc-actgt-gggtggcaagatagtgggctctctgtgtgccattgcgggc 1146
```

```
            |||||  ||  |  |  ||   |  |||  ||  ||||||||||  ||  ||  |||||  |||||  ||
Sbjct: 50516 catggttcc-gactaccattggg-ggaaagatagtgggttccctatgtgcgattgcaggt 50459


Query: 1147  gtgctgactatttccctgccagtgccc-gtcattgtctccaatttcagctacttttatca 1205
              |||  |  ||||||  ||  |  ||  ||  |||  ||||||||  ||||||||||  ||||||  ||  ||
Sbjct: 50458 gtgttaactattgccttaccggt-ccctgtcattgtgtccaatttcaactacttctacca 50400


Query: 1206  ccgggagacagaggg 1220
              ||||||||||||||
Sbjct: 50399 ccgggagacagaggg 50385



 Score = 77.8 bits (39), Expect = 2e-11
 Identities = 62/69 (89%), Gaps = 3/69 (4%)
 Strand = Plus / Minus


Query: 162    cgagtatttcttcgaccggc-accggcccagcttcgacgccgtgctctactactaccagt 220
              ||||||  ||||||||||  ||  ||||||||||||||||||  |  ||||||||||  ||||
Sbjct: 121245 cgagtacttcttcgacc-gcaaccggcccagcttcgacgccatcctctactactatcagt
121187


Query: 221    ccggtgggc 229
              ||||  ||||
Sbjct: 121186 ccgg-gggc 121179



>AC006063.1.1.150001
          Length = 150001

 Score = 93.7 bits (47), Expect = 3e-16
 Identities = 75/84 (89%), Gaps = 2/84 (2%)
 Strand = Plus / Minus


Query: 162   cgagtatttcttcgaccggc-accggcccagcttcgacgccgtgctctactactaccagt 220
              ||||||  ||||||||||  ||  ||||||||||||||||||  |  ||||||||||||||||
Sbjct: 55998 cgagtacttcttcgacc-gcaaccggcccagcttcgacgccatcctctactactaccagt 55940


Query: 221   ccggtgggcggctgcggcggccgg 244
              ||||  ||  ||  ||||||  ||||||
Sbjct: 55939 ccggcggccgcctgcggaggccgg 55916



>AL358215.16.1.101529
          Length = 101529

 Score = 83.8 bits (42), Expect = 3e-13
 Identities = 153/189 (80%), Gaps = 6/189 (3%)
 Strand = Plus / Minus


Query: 813   catgtcactggccatcctgagag-tcatccgattggtgcgtgtcttccgcatcttcaagc 871
              ||||||  ||||||||||||||  |  |||||||  |||||  |  ||||||||||||||||||
```

```
Sbjct: 64185 catgtccctggccatcctgag-gatcatccgcctggtgagggtcttccgcatcttcaagc 64127


Query: 872   tgtcccggcactcaaagggcctgcaaatctt-gggccagacgcttcgggcctccatgcgt 930
              | || || ||||| ||||| ||||| ||| | |||| | || ||   ||| ||||||||
Sbjct: 64126 tctcgcgccactccaaggggctgcagatcctcgggcaa-acactgaaggcgtccatgcgg 64068


Query: 931   gagctgggcctcctcatctt-tttcctcttcatcggtgtggtcctcttttccagcgccgt 989
              ||| ||||  | |||||||| |||| ||||||| || ||  ||||||| ||||| || ||
Sbjct: 64067 gagttggggttgctcatcttctttc-tcttcattggagtcatcctcttctccagtgcagt 64009


Query: 990   ctactttgc 998
              |||||||||
Sbjct: 64008 ctactttgc 64000
```